

WHAT IS CLAIMED IS:

1. A non-naturally-occurring polypeptide having an amino acid sequence sufficiently duplicative  
5 of that of naturally-occurring stem cell factor to allow possession of a hematopoietic biological activity of naturally occurring stem cell factor.

2. A purified polypeptide comprising  
10 naturally-occurring stem cell factor.

3. A polypeptide according to Claim 1 or 2 wherein said polypeptide is the product of procaryotic or eukaryotic expression of an exogenous DNA sequence.  
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4. A polypeptide according to Claim 3 wherein said polypeptide is the product of CHO cell expression.

5. A polypeptide according to Claim 3 wherein the exogenous DNA sequence is a cDNA sequence.  
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6. A polypeptide according to Claim 1 or 2 wherein said stem cell factor is human stem cell factor.  
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7. A polypeptide according to Claim 3 wherein the exogenous DNA sequence is a genomic DNA sequence.

8. A polypeptide according to Claim 3 wherein the exogenous DNA sequence is carried on an autonomously replicating DNA plasmid or viral vector.  
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9. A polypeptide according to Claim 1 possessing part or all of the amino acid sequence of human stem cell factor as set forth in Figure 15B, Figure 15C, Figure 42 or Figure 44 or any naturally-  
5 occurring allelic variant thereof.

10. A polypeptide according to Claim 1 which has an in vivo biological activity of naturally-  
occurring stem cell factor.

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11. A polypeptide according to Claim 1 which has an in vitro biological activity of naturally-  
occurring stem cell factor.

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12. A polypeptide according to Claim 1 or 2 further characterized by being covalently associated with a detectable label substance.

13. An isolated DNA sequence for use in  
20 securing expression in a procaryotic or eukaryotic host cell of a polypeptide product having an amino acid sequence sufficiently duplicative of that of naturally-  
occurring stem cell factor to allow possession of a hematopoietic biological activity of naturally occurring  
25 stem cell factor, said DNA sequence selected from among:

(a) DNA sequences set out in Figure 14B, Figure 14C, Figure 15B, Figure 15C, Figure 42, Figure 44, or their complementary strands;

(b) DNA sequences which hybridize to the DNA  
30 sequences defined in (a) or fragments thereof; and

(c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).

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14. A procaryotic or eukaryotic host cell transformed or transfected with a DNA sequence according to Claim 13 in a manner allowing the host cell to express said polypeptide product.

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15. A polypeptide product of the expression of a DNA sequence of Claim 13 in a procaryotic or eukaryotic host cell.

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16. An isolated DNA sequence coding for procaryotic or eukaryotic host expression of a polypeptide having an amino acid sequence sufficiently duplicative of that of naturally occurring stem cell factor to allow possession of a hematopoietic biological activity of naturally-occurring stem cell factor.

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17. A cDNA sequence according to Claim 16.

18. A genomic DNA sequence according to Claim 16.

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19. A DNA sequence according to Claim 16 wherein said DNA sequence codes for human stem cell factor.

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20. A DNA sequence according to Claim 19 and including one or more codons preferred for expression in E. coli cells.

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21. A DNA sequence according to Claim 16 having the sequence set out in Figure 15B, Figure 15C, Figure 42 or Figure 44.

22. A DNA sequence according to Claim 16 and including one or more codons preferred for expression in yeast cells.

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23. A DNA sequence according to Claim 16 covalently associated with a detectable label substance.

24. A DNA sequence coding for a polypeptide fragment or polypeptide analog of naturally-occurring stem cell factor.

25. A DNA sequence as in Claim 24 coding for methionyl stem cell factor.

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26. A biologically functional plasmid or viral DNA vector including a DNA sequence according to Claim 16.

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27. A procaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to Claim 26.

28. A polypeptide product of the expression in a procaryotic or eukaryotic host cell of a DNA sequence according to Claim 16.

29. A polypeptide having part or all of the amino acid sequence as set forth in Figure 15C, Figure 42 or Figure 44 and having one or more of the in vitro biological activities of naturally-occurring stem cell factor.

30. A polypeptide having part or all of the secondary conformation of naturally-occurring stem cell factor and having part or all of the amino acid sequence set forth in Figure 15C, Figure 42, or Figure 44 and having a biological property of naturally-occurring human stem cell factor.

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31. A process for the production of stem cell factor comprising:

growing, under suitable nutrient conditions, procaryotic or eukaryotic host cells transformed or  
5 transfected with a DNA according to Claim 13, and isolating desired polypeptide products of the expression of DNA sequences in said vector.

32. A composition comprising a purified and  
10 isolated human stem cell factor free of association with any human protein in glycosylated or nonglycosylated form.

33. A pharmaceutical composition comprising  
15 an effective amount of a polypeptide according to Claim 1 and a pharmaceutically-acceptable diluent, adjuvant or carrier.

34. A method for treatment of leucopenia in a  
20 mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

35. A method for treatment of  
25 thrombocytopenia in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

30 36. A method for treating anemia in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

37. A method for enhancing engraftment of  
35 bone marrow during transplantation in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

38. A method of enhancing bone marrow recovery in treatment of radiation, chemical, or chemotherapeutic induced bone marrow aplasia or myelosuppression which comprises treating patients with therapeutically effective doses of stem cell factor.

39. A DNA sequence coding for an analog of human stem cell factor selected from the group consisting of:

- a) [Met<sup>-1</sup>] stem cell factor; and
- b) stem cell factor wherein one or more cysteines are replaced by alanine or serine.

40. A polypeptide product of the expression in a procaryotic or eukaryotic host cell of a DNA sequence according to Claim 39.

41. A pharmaceutical composition comprising recombinant stem cell factor having the human amino acid sequence, and a pharmaceutically acceptable diluent, adjuvant or carrier.

42. An antibody specifically binding stem cell factor.

43. An antibody as in Claim 42 wherein said antibody is a monoclonal antibody.

44. A process for the efficient recovery of stem cell factor from SCF containing material, the method comprising the step of subjecting the SCF containing material to ion exchange chromatographic separation.

45. A process as in Claim 44 wherein said ion exchange chromatographic separation is anion exchange chromatographic separation.

5           46. A process as in Claim 44 further comprising the step of reverse phase liquid chromatographic separation.

10           47. A process for the efficient recovery of stem cell factor from SCF containing material, the method comprising the step of subjecting the SCF containing material to reverse phase liquid chromatographic separation.

15           48. A polypeptide having the hematopoietic biological activity of naturally occurring stem cell factor, said polypeptide having an amino acid sequence set forth in Figure 15C, Figure 42 or Figure 44 or any allelic variants, derivatives, deletion analogs,  
20           substitution analogs, or addition analogs thereof, and characterized by being the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.

            49. A polypeptide as in Claim 48 selected  
25           from the group consisting of:  
            SCF<sup>2</sup>-164, SCF<sup>5</sup>-164, SCF<sup>1</sup>-130,  
            SCF<sup>1</sup>-148, SCF<sup>1</sup>-162, SCF<sup>1</sup>-164, SCF<sup>1</sup>-165, SCF<sup>1</sup>-183  
            (Figure 15C); SCF<sup>1</sup>-185, SCF<sup>1</sup>-188, SCF<sup>1</sup>-189, and SCF<sup>1</sup>-248  
            (Figure 42); and SCF<sup>1</sup>-157, SCF<sup>1</sup>-160, SCF<sup>1</sup>-161 and  
30           SCF<sup>1</sup>-220 (Figure 44).

            50. A biologically active composition comprising the polypeptide of Claim 1 covalently attached to a water-soluble polymer.

51. A composition as in Claim 50 wherein said polymer is selected from the group consisting of polyethylene glycol or copolymers of polyethylene glycol and polypropylene glycol, and said polymer is  
5 unsubstituted or substituted at one end with an alkyl group.

52. The composition of Claim 50 wherein the polypeptide is [Met<sup>-1</sup>] SCF<sup>1-164</sup>.

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53. The composition of Claim 50 wherein said polymer has an average molecular weight of about 1,000 to 100,000 daltons.

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54. The composition of Claim 50 wherein said polymer has an average molecular weight of about 4,000 to 40,000 daltons.

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55. The composition of Claim 50 wherein said polymer is an unsubstituted polyethylene glycol or a monomethoxy polyethylene glycol.

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56. The composition of Claim 50 wherein said polymer is attached to said polypeptide via reaction with an active ester of a carboxylic acid or carbonate derivative of said polymer.

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57. The composition of Claim 50 wherein one or more amino groups of said protein are conjugated to said polymer by reaction with a N-hydroxysuccinimide, p-nitrophenol or 1-hydroxy-2-nitro-benzene-4-sulfonate ester of the polymer.

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58. The composition of Claim 50 wherein one or more free cysteine sulfhydryl groups are conjugated to said polymer via reaction with a malimido or haloacetyl derivative of the polymer.



59. The composition of Claim 50 wherein the polypeptide is glycosylated and the polymer is attached by reaction of an amino, hydrazine or hydrazide derivative of the polymer with one or more aldehyde groups generated by oxidation of the carbohydrate moieties.

60. A method for preparing a biologically active polymer-polypeptide adduct which comprises reacting the polypeptide of Claim 50 with a water-soluble polymer under conditions permitting the covalent attachment of the polymer to said polypeptide, and recovering the adduct so produced.

61. A method of treating acquired immune deficiency in a human comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

62. A method of treating neoplasia in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

63. A method as in Claim 62 wherein before said administering step is the step of administering chemotherapy or irradiation to said mammal.

64. A method of transfecting early hematopoietic progenitor cells with a gene comprising:  
(i) culturing early hematopoietic progenitor cells with SCF; and  
(ii) transfecting the cultured cells of step (i) with a gene.

65. A method of transferring a gene to a mammal comprising the steps of:

(i) culturing early hematopoietic progenitor cells with SCF;

5 (ii) transfecting the cultured cells of step (i) with a gene; and

(iii) administering the transfected cells to said mammal.

10 66. A method of treating nerve damage in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

15 67. A method of treating infertility in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

20 68. A method of treating intestinal damage in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

25 69. A method of treating myeloproliferative disorder in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1 conjugated to a toxin.

30 70. A polypeptide as in Claim 48 selected from the group consisting of:

[Met<sup>-1</sup>]SCF<sup>1</sup>-148, [Met<sup>-1</sup>]SCF<sup>1</sup>-162,  
[Met<sup>-1</sup>]SCF<sup>1</sup>-164, [Met<sup>-1</sup>]SCF<sup>1</sup>-165, [Met<sup>-1</sup>]SCF<sup>1</sup>-183  
(Figure 15C); [Met<sup>-1</sup>]SCF<sup>1</sup>-185, [Met<sup>-1</sup>]SCF<sup>1</sup>-188,  
35 [Met<sup>-1</sup>]SCF<sup>1</sup>-189, and [Met<sup>-1</sup>]SCF<sup>1</sup>-248 (Figure 42); and  
[Met<sup>-1</sup>]SCF<sup>1</sup>-157, [Met<sup>-1</sup>]SCF<sup>1</sup>-160, [Met<sup>-1</sup>]SCF<sup>1</sup>-161 and  
[Met<sup>-1</sup>]SCF<sup>1</sup>-220 (Figure 44).